

REMARKS

Claims 1, 18-27, and 30-46 are pending in the application. Claim 30 has been amended so that it no longer depends from a canceled claim. No new matter has been added.

Applicants note the withdrawal of the prior rejections on page 2 of the Office action, and turn now to the rejections maintained or newly made in the present Office action.

35 U.S.C. § 112, ¶ 2

Claims 37 and 46 were rejected as being indefinite (Office action at page 3). The Examiner states, “[i]n claims 37 and 46, it is not clear what proteins are encompassed by an amyloid-associated protein” (Office action at page 3, ¶ 8).

This ground for rejection is respectfully traversed. The term “amyloid-associated protein” is a term routinely used in this art, and one of ordinary skill would know, or would be able to determine whether, a given protein is an amyloid-associated protein. In support of this statement, Applicant searched the database commonly referred to as “PubMed,” which is available through the National Center for Biotechnology Information at www.ncbi.nlm.nih.gov. The search query “amyloid-associated protein” run on today’s date produced 151 “hits,” the first twenty of which are attached as **Exhibit A**. The Examiner’s attention is directed toward #7, where the term “[a]myloid associated proteins” appears in the article’s title. In view of the evidence that those of ordinary skill in the art routinely use and would understand the term “amyloid-associated protein” and that these practitioners would, therefore, understand the metes and bounds of claims 37 and 46, the Examiner is respectfully asked to reconsider and withdraw this ground for rejection.

Claims 31-33 were “rejected for depending on rejected claim 30” (Office action at page 3, ¶ 9). Claim 30, from which claims 31-33 depend, has been amended so that it no longer depends from canceled claim 28. In view of this amendment, the present ground for rejection should be withdrawn.

35 U.S.C. § 103

Claims 1, 18-22, 24-26, 34-36, and 38-44 were rejected as being obvious over Burke *et al.* (U.S. Patent No. 6,632,616; herein, "the '616 patent") and Ladner *et al.* (U.S. Patent No. 4,946,778; herein, "the '778 patent") (Office action at pages 3-6). Claims 1, 18-27, 34-36, and 38-46 were rejected as being obvious over the '616 patent in view of the '778 patent and further in view of Housman *et al.* (U.S. Patent No. 6,420,122; herein, "the '122 patent").

This ground for rejection should be withdrawn in view of the Declaration of Dr. Leslie Thompson, which is attached as **Exhibit B**, and which establishes that a therapeutic agent, as now claimed, was reduced to practice prior to the earliest effective date of the '616 patent. The Declaration is submitted in accordance with 37 C.F.R. 1.131 to establish that the present Applicants invented the therapeutic agent now claimed prior to the earliest possible effective date of the '616 patent. The '616 patent claims the benefit of a provisional application filed on March 16, 2000, which is only approximately five months earlier than the filing date of the provisional application to which the current application claims the benefit of priority. The '616 patent cannot, therefore, qualify as prior art under 35 U.S.C. § 102(b) and can be removed as a reference by Applicants' showing of a reduction to practice prior to March 16, 2000.

As stated, in the attached Declaration, prior to March 16, 2000, Dr. Thompson worked with others at the University of California – Irvine to develop an animal model that could be used to screen and identify therapeutic agents useful in ameliorating diseases, such as Huntington's Disease, which are associated with undesirable protein-protein interactions within affected cells (Declaration at ¶ 2). Some of the work performed to generate that animal model was described in an article entitled, "Expanded polyglutamine peptides alone are intrinsically cytotoxic and cause neurodegeneration in *Drosophila*", which was published in *Human Molecular Genetics*, 9(1):13-25, 2000 (Declaration at ¶ 2). The manuscript was received by the journal on August 23, 1999 (Declaration at ¶ 2).

Prior to March 16, 2000, Dr. Thompson also worked with others at the University of California – Irvine to test therapeutic agents in the animal model described above (Declaration at ¶ 3). As described in Example 2 of the application, co-expression of (1) an expanded

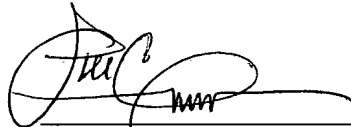
polyglutamine repeat peptide and (2) an agent designed to inhibit aggregation of the repeat peptide, reduced lethality in *Drosophila* (Declaration at ¶ 3). The same therapeutic agent rescued degenerating neurons in the *Drosophila* eye (Declaration at ¶ 3). One of the therapeutic agents tested in Example 2 is referred to as H3/H4 because it includes a domain that consists of a polypeptide comprising two of the alpha-helical regions (H3 and H4) of the tata-binding protein (see Figure 1 of the specification) (Declaration at ¶ 3). The alpha-helical regions constitute the "third domain" as they separate a first domain that binds a first protein and a second domain that binds a second protein (Declaration at ¶ 3).

Given that a therapeutic agent as now claimed was reduced to practice prior to the earliest possible effective date of the '616 patent, Applicants contend that the '616 patent cannot serve as a basis for the current rejection. As the Examiner has not presented arguments that either the '778 patent alone or the '778 patent in combination with the '122 patent can support a *prima facie* case of obviousness without the '616 patent, this ground for rejection must be withdrawn.

Enclosed is a Petition for Extension of Time and a check for the required fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: November 29, 2005



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All: 151 Review: 23

Items 1 - 20 of 151

Page 1 of 8 Next

☐ 1: [Gopalan SM, Wilczynska KM, Konik BS, Bryan L, Kordula T.](#) Related Articles, Links

Astrocyte-specific expression of the alpha 1-antichymotrypsin and glial fibrillary acidic protein genes requires activator protein-1.
J Biol Chem. 2005 Nov 22; [Epub ahead of print]
PMID: 16303762 [PubMed - as supplied by publisher]

☐ 2: [Gazit E.](#) Related Articles, Links

Mechanisms of amyloid fibril self-assembly and inhibition.
FEBS J. 2005 Dec;272(23):5971-8.
PMID: 16302962 [PubMed - in process]

☐ 3: [Naiki H, Yamamoto S, Hasegawa K, Yamaguchi I, Goto Y, Gejyo E.](#) Related Articles, Links

Molecular interactions in the formation and deposition of beta2-microglobulin-related amyloid fibrils.
Amyloid. 2005 Mar;12(1):15-25. Review.
PMID: 16076607 [PubMed - indexed for MEDLINE]

☐ 4: [Saura CA, Chen G, Malkani S, Choi SY, Takahashi RH, Zhang D, Gouras GK, Kirkwood A, Morris RG, Shen J.](#) Related Articles, Links

Conditional inactivation of presenilin 1 prevents amyloid accumulation and temporarily rescues contextual and spatial working memory impairments in amyloid precursor protein transgenic mice.
J Neurosci. 2005 Jul 20;25(29):6755-64.
PMID: 16033885 [PubMed - in process]

☐ 5: [Miao J, Vitek MP, Xu F, Previti ML, Davis J, Van Nostrand WE.](#) Related Articles, Links










Reducing cerebral microvascular amyloid-beta protein deposition diminishes regional neuroinflammation in vasculotropic mutant amyloid precursor protein transgenic mice.
J Neurosci. 2005 Jul 6;25(27):6271-7.
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☐ 6: [Saba M, Tohme A, Abadjian G, Haddad F, Ghayad E.](#) Related Articles, Links

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Activation of human microglia by fibrillar prion protein-related peptides is enhanced by amyloid-associated factors SAP and C1q.
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Anti-Abeta antibody treatment promotes the rapid recovery of amyloid-associated neuritic dystrophy in PDAPP transgenic mice.
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Presurgical plasma exchange is ineffective in correcting amyloid associated factor X deficiency.
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Trace metal contamination initiates the apparent auto-aggregation, amyloidosis, and oligomerization of Alzheimer's Abeta peptides.
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PMID: 15459123 [PubMed - indexed for MEDLINE]
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 **Atomic force microscopy reveals defects within mica supported lipid bilayers induced by the amyloidogenic human amylin peptide.**
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- ☐ **19:** [Zhu LC, Sidhu GS, Yee HT, Cassai ND, Goldfarb DS, Wiczorek RL.](#) [Related Articles, Links](#)
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- ☐ **20:** [Rogers JT, Lahiri DK.](#) [Related Articles, Links](#)
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Page

1

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